IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **A. Palani *et al.***	:	
Serial No.: **10/629,466**	:	Examiner: Celia C. Chang
Filed: **July 29, 2003**	:	Group Art Unit: 1625
For: **"PIPERIDINE DERIVATIVES USEFUL AS CCR5 ANTAGONISTS**	:	Date: December 20, 2007

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132 OF MICHAEL W. MILLER, Ph.D.

I, Michael W. Miller, declare as follows:

1. I am an inventor of the subject matter claimed in the above-referenced patent application.

2. I received a Ph.D. degree in Chemistry from Colorado State University in 1994. I have been working as a scientist for over 10 years. I am the author of 13 publications, am an inventor in at least 5 granted US patents, have given a number of scientific presentations, and have received numerous honors/awards. Currently, I am employed as a Senior Principal Scientist at Schering-Plough Research Institute.

3. I have read the references (US 2004/0142920 and GB 018876.4) at issue in the Office Action dated June 20, 2007 for the above captioned patent application.

4. I have previously submitted a Declaration on March 8, 2007 in connection with the present application, which is incorporated herein by reference in its entirety.

5. I further make the following statements with regard to the data provided in above-mentioned declaration.

6. In comparing the reference compound with the compound of example 72, only one structural difference is seen, viz., replacement of the dimethylphenyl with dimethylpyrimidyl. In Table 2 of the Declaration, it is seen that the shift in antiviral activity with increase in human serum level is approximately of the same order of magnitude for both the reference compound (44/0.90=48.9 fold shift) and the compound of example 72 (32/0.95=33.4 fold shift), i.e., there is only about 1.5 fold (48.9/33.4= 1.5) change in magnitude in the shift of antiviral activity between the reference compound and the compound of example 72.

7. However, in going from the compound of example 72 to the compound of example 9, where the only structural difference is the replacement of the phenyl in the compound of example 72 with the benzyl group in the compound of example 9, a much more striking difference in the shift in antiviral activity with increase in human serum level is seen. The compound of example 9 shows a shift of only about 3.3 (1.7/0.52=3.3) in antiviral activity compared to the 33.4 fold shift for the compound of example 72. In other words, the antiviral activity of the compound of example 9 changes much less (about 11

fold less) than the compound of example 72 in the presence of increasing amount of human serum.

8. Therefore, I conclude that this unexpected difference in the antiviral activity between the compound of example 9 and the compound of reference 72 is due to replacement of the phenyl group on the N atom in the compound of example 72 to the benzyl group in the compound of example 9.

9. Furthermore, based on the data provided in the Declaration, I also conclude that, in comparing the reference compound with the compound of example 9, it is the replacement of the nitrogen phenyl with the nitrogen benzyl, rather than the replacement of the dimethylbenzyl with dimethylpyrimidyl that is primarily responsible for the unexpected shift in antiviral activity.

10. I maintain my conclusion that the compound of Example 9 would be favored based on the reduced plasma protein binding and the unexpected reduction in shift in antiviral activity in human plasma. This compound should be expected to interact with the desired receptor (CCR5) with higher efficiency *in-vivo*. Structurally, this compound corresponds to presently claimed Formula I wherein R^2 is arylalkyl and R^3 is substituted pyrimidine. Thus, present compounds with these structural features are expected to have unexpected beneficial features, as shown by the compound of Example 9. Furthermore, these structural features are absent from the reference compound.

11. All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false

statements and the like so made are punishable by fine or imprisonment or both under 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of the application and any patent issued thereon.

December 20 2007

Date

Michael W. Miller, Ph. D.